

Attorney Docket No.: KUZ0032US.NP
Inventors: Hashimoto et al.
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REMARKS

Claims 1-7 and 11 are pending in the instant application. Claims 1-7 and 11 have been rejected. Claim 1 has been amended. Claims 4 through 6 have been canceled in light of the amendment to claim 1. New claims 12-15 have been added. Support for these amendments is provided by canceled claims 4 through 6, original claims 8-10 and claim 3. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejections of Claims 1-7 and 11 under 35 U.S.C 103(a)

The rejection of claims 1-7 and 11 under 35 U.S.C. 103(a) as being unpatentable over Tsuruda et al. (WO 01/68061 in view of Honda (U.S. Patent 5,637,293) has been maintained.

The rejection of claims 1-7 and 11 under 35 U.S.C. 103(a) as being unpatentable over Tsuruda et al. (WO 01/68061 in view of Yasukochi et al. (U.S. Patent Application Publication No. 2005/0053646) has also been maintained.

The rejection of claims 1-4, 6, 7 and 11 have been rejected under 35 U.S.C. 103(a) as being unpatentable over

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US 2003/0109819 (hereinafter '819) in view of Tateishi has also been maintained

Further, claim 5 has been rejected under 35 U.S.C. 103(a) as being unpatentable over '819 in view of Tateishi as applied to claim 1-4, 6, and 7-11 and further in view of Honda.

Applicants respectfully traverse these rejections.

Claim 1 has been amended to recite a patch preparation comprising a support and an adhesive base, the adhesive base containing 8 to 50 mass % relative to total amount of the adhesive base of a rubber-system macromolecule having a double bond at least in a principal chain thereof and 0.1 to 10 mass % relative to entire amount of the preparation of a nonsteroidal anti-inflammatory analgesic drug, and the adhesive base further containing 0.5 to 20 mass % relative to entire amount of the preparation of 4-tert-butyl-4'-methoxydibenzoylmethane as a stabilizer for the rubber-system macromolecule.

MPEP 2143.02 is clear; a rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective

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functions, and the combination would have yielded **nothing more than predictable results** to one of ordinary skill in the art (emphasis added). *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1395 (2007); *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). To establish a case of prima facie obviousness, at least some degree of predictability is required. See MPEP 2143.02.

The cited combinations of references do not provide any predictability with respect to the instant claimed invention.

For example, the Examiner has acknowledged that Tsuruda et al. does not teach the UV blocker in the adhesive base. The Examiner suggests that "Tsuruda et al. clearly establishes that incorporating UV absorbent into the base was common practice in the art at the time of the invention. In support of this suggestion, the Examiner quotes col. 1 lines 39-41 of Tsuruda et al. as stating "the means for keeping the stability of a medicine in patches has generally been to incorporate an ultraviolet absorbent into the base."

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However, that is not the entire teaching. At col. 1, lines 39-44, Tsuruda et al. states "the means for keeping the stability of a medicine in patches has generally been to incorporate an ultraviolet absorbent into the base, **but there has remained a problem to be worried about as to safety and the like due to said absorbent's direct contact with or absorption into the skin** (emphasis added). MPEP 2141.03 is clear; a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Applicants believe the teachings of Tsuruda et al., when read in their entirety as required by MPEP 2141.03, actually lead the skilled artisan to question predictability with respect to inclusion of a UV blocker in the adhesive base of a patch.

Honda also states at col. 1, lines 54-57 that "ultraviolet light absorbents have a problem with solubility and separate out in preparation, and fail to fully exhibit their ultraviolet light-absorbing ability, leading to a deteriorated stability of kojic acid." Honda solved this problem by combining kojic acid and an ultraviolet light

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absorbent with a fatty acid ester or a fatty acid glyceride. See teachings in Honda at col. 2, lines 11-20. Accordingly, this reference is also in no way predictive of solubility and separation and thus utility of a patch containing the ultraviolet absorbent 4-tert-butyl-4'-methoxydibenzoylmethane in an adhesive base comprising a rubber-system macromolecule having a double bond at least in a principal chain thereof and a non-steroidal antiinflammatory agent as claimed.

Teachings of Yasukochi et al. relate to an adhesive of aqueous and nonaqueous polymers for holding lipophilic drugs which is crosslinked with a boron compound to enhance tackiness and cohesiveness. This reference is also in no way predictive of safety, solubility and/or separation and thus utility of a patch containing 4-tert-butyl-4'-methoxydibenzoylmethane in an adhesive base comprising a rubber-system macromolecule having a double bond at least in a principal chain thereof and a non-steroidal antiinflammatory agent as claimed.

US 2003/0109819 is acknowledged by the Examiner not to disclose the percentage of UV absorbent useful in the invention. Nor does this reference teach the ultraviolet absorbent 4-tert-butyl-4'-methoxydibenzoylmethane.

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Accordingly, this reference is also in no way predictive of safety, solubility and/or separation and thus utility of a patch containing 4-tert-butyl-4'-methoxydibenzoylmethane in an adhesive base comprising a rubber-system macromolecule having a double bond at least in a principal chain thereof and a non-steroidal antiinflammatory agent as claimed.

Finally, teachings of Tateishi are focused on the laminated backing layer onto which a drug-containing pressure sensitive adhesive layer is laminated. Accordingly, this reference is also in no way predictive of safety, solubility and/or separation and thus utility of a patch containing 4-tert-butyl-4'-methoxydibenzoylmethane in an adhesive base comprising a rubber-system macromolecule having a double bond at least in a principal chain thereof and a non-steroidal antiinflammatory agent as claimed.

Without any predictability, the cited combinations of references fail to establish a prima facie case of obviousness. See MPEP 2143.02.

Further, MPEP 2141.02 states "[a]scertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering both the invention and the prior art references as a whole." In determining the differences between the prior art and the

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claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). Applicants believe that the cited combinations of references in these 103 rejections fail to consider the teachings of each reference as a whole. For example, citing Honda simply for its listing both dibenzoylmethane derivatives and benzotriazole derivative as ultraviolet light absorbents useful in their invention fails to take into consideration the teachings of this reference as a whole. Honda when viewed in its entirety is unrelated to transdermal patches with adhesive bases, unrelated to anti-inflammatory agents and requires a fatty acid ester or fatty acid glyceride not required by the present invention. Simply because Honda lists both dibenzoylmethane derivatives and benzotriazole derivative as ultraviolet light absorbents useful in their invention is in no way predictive of use of these ultraviolet absorbents in the instant claimed invention. Similarly, citing Yasukochi simply because it teaches UV absorbing agents in an amount of 15 wt. % or less fails to take into consideration the teachings of this

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reference as a whole. Yasukochi et al. is focused on enhancing tackiness and cohesiveness of aqueous and nonaqueous polymers holding lipophilic drugs via crosslinkage with a boron compound. Yasukochi when viewed in its entirety is unrelated to the instant claimed transdermal patches where crosslinkage and lipophilicity of the drug are not concerns. Simply because Yasukochi et al. teaches a similar concentration for ultraviolet light absorbents in their invention, it is not predictive of use of these ultraviolet absorbents in the instant claimed invention.

MPEP 2143.01 is clear; the mere fact that references can be combined or modified does not render the resultant combination obvious unless **>the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007). In an earnest effort to advance the prosecution of this case, Applicants are providing herewith a Declaration by co-inventor Dr. Tsuruda demonstrating unpredicted and/or unexpected advantages of a composition comprising 4-tert-butyl-4'-methoxydibenzoylmethane. Specifically, experiments were performed in mice comparing compositions containing ketoprofen and either 3% 4-tert-

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butyl-4'-methoxydibenzoylmethane (BM-DBM) or 3% Mexoryl® XL (a hydroxybenzotriazol derivative obtained from Nihon L'Oreal, Inc.). See paragraph 2 of Dr. Tsuruda's Declaration. These compositions were applied to the ears of mice, followed by irradiation of 40 J/cm² of UVA. See paragraph 2 of Dr. Tsuruda's Declaration. Measurement of the thicknesses of the ears after 24 hours irradiation showed solutions containing 3% BM-DMA to significantly suppress the increase in ear thickness indicative of swelling as compared to solutions containing 3% Mexoryl® XL (a hydroxybenzotriazol derivative obtained from Nihon L'Oreal, Inc.). See paragraph 3 and Figure 1 of Dr. Tsuruda's Declaration. The data thus clearly shows that ketoprofen phototoxicity is reduced significantly more by using 4-tert-butyl-4'-methoxydibenzoylmethane (BM-DBM) as claimed than with a hydroxybenzotriazol derivative - UV blockers suggested to be equivalents by the Examiner.

The evidence submitted via this Declaration of superior and unexpected properties of the instant claimed invention rebuts any prima facie of obviousness over the cited combinations of references. See MPEP 2145.

Withdrawal of these rejections under 35 U.S.C. 103 is respectfully requested.

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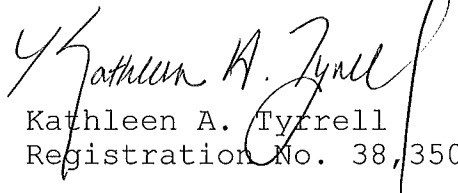
II. Rejection of Claims 4-6 under 35 U.S.C. 112, first paragraph

Claims 4-6 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. It is respectfully pointed out that these claims have been canceled, thus rendering moot this rejection. Withdrawal of this rejection is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,


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